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10/783,054	02/20/2004	Ashutosh Chilkoti	5405-318	6784
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MYERS BIGEL SIBLEY & SAJOVEC PO BOX 37428 RALEIGH, NC 27627				
EXAMINER				
HELM, CARALYNNE E				
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/783,054

**Applicant(s)**

CHILKOTI ET AL.

**Examiner**

CARALYNNE HELM

**Art Unit**

1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 18 August 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-9 and 11-50 is/are pending in the application.
- 4a) Of the above claim(s) 3, 15, 20, 22-27 and 47 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4-9, 11-14, 16-19, 21, 28-46 and 48-50 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Election/Restrictions***

To summarize the current election, applicants elected where the article is an orthopedic implant, the protein-resistant head group is tri(sarcosine), and the surface portion comprises metal.

Claims 3, 15, 20, 22-27, and 47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim.

## **NEW REJECTIONS**

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The four factual inquiries of *Graham v. John Deere Co.* have been fully considered and

analyzed in the rejections that follow.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 4-9, 11-14, 16, 18-19, 21, 32-39, 41-46, 48, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chapman et al. (previously cited) view of Hawker et al. (previously cited), and Zhang et al. (previously cited).

Broadly, the invention of claims 1-2, 4, 6-9, 12-14, 18, 21, and 32 is a device (article) with polymer brushes on its surface that are attached to the device surface via a linking layer. These polymer brush bristles have protein resistant groups (kosmotropes) that confer protein resistance to the surface of the device. Chapman et al. teach this concept (see figure 1 and paragraphs 114-117; instant claim 1). A self assembled monolayer of alkanethiol is formed on an article that is coated with gold (see paragraph 153 and 159; instant claims 2, 4 and 6). The exposed end is converted into a reactive functional group (initiator terminated alkanethiol) such that a polymer can be grafted (see paragraph 153; instant claim 7). This polymer contains several head groups

(branches) that resist the adsorption of proteins (see paragraph 153 and 162).

Functional groups other than the acetoamido groups exemplified are taught to also serve as head groups on the polymer (see paragraph 115 and 196). Chapman et al. teach such coatings for articles that are in-dwelling, such as artificial bone or joint replacements (orthopedic implant) (see paragraph 64; instant claim 21). Chapman et al. also teach self assembled monolayers that display different protein resistant head groups. In the set demonstrated to be particularly effective is tri(sarcosine) (see figures 4-5 and paragraph 144; instant claims 12-14). Chapman et al. go on to teach that in addition to protein resistance, their polymer layers can be further modified by covalently attaching ligands that bind specific biomolecules (receptor) (see paragraph 124; instant claim 18-19). Protein molecules are particularly envisioned (see paragraph 121; instant claim 18). Upon exposure to fluid with biomolecules, adsorption of general biomolecules (e.g. protein) is resisted such that only binding of those biomolecules for which the ligand is specific occurs (see paragraph 124; instant claim 32).

Claims 1 and 8-9 recite a product-by-process. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) see MPEP 2113. In the instant case, these claims do not add any structural limitation to the invention. Thus in view of the teachings of Chapman et al., it

would have been obvious to one of ordinary skill in the art at the time of the invention to select tri(sarcosine) as the protein resistant head group to include in the surface bound polymer of their invention, where an orthopedic implant is the coated article and gold is in the metal layer linking the polymer to the article substrate. Further the use of their invention where a protein capable of binding a particular biomolecule is attached to the polymer to selectively capture this biomolecule from a biological fluid, while repelling the binding of other proteins, would also have been obvious based upon the teachings of Chapman et al. Therefore, Chapman et al. make obvious an orthopedic device with a gold linking layer to which is attached a polymer brush with tri(sarcosine) as head groups on its bristles. This reference does not explicitly teach that the polymer is formed of monomers with a vinyl core monomer group and a protein resistant head group coupled thereto, produced via surface initiated polymerization, or that the linking layer is patterned on the substrate.

Zhang et al. teach a polymer brush utilized to resist protein adhesion on implant surfaces (see page 691 column 1 paragraph 10). Specifically these polymers are composed of monomers of methacryloyloxyethyl phosphorylcholine, an acrylate monomer with a coupled phosphorylcholine group, and butyl methacrylate (see page 691 column 2 paragraph 1 and page 700 column 1 paragraph 2; instant claims 10-11 and 42-43). Chapman et al. teach phosphorylcholine as an envisioned protein resistant head group whose performance in this capacity was not as good as tri(sarcosine) (see Chapman et al. figure 5).

Hawker et al. teach polymer brush patterns built from a self assembled monolayer on a substrate (see abstract; instant claims 38). In particular, a substrate surface that can be composed of a variety of envisioned materials (e.g. gold or tungsten) serves as the base for the polymer (see column 8 lines 9-18; instant claims 34-35). Subsequently a compound (linking layer) containing a group reactive with the substrate surface on one end and providing an initiator on the other end is applied to the surface (see column 8 lines 56-67 and column 9 lines 27-29). The material is then contacted with a polymerizable composition composed of monomers that sequentially form polymers at these initiation sites (see column 9 lines 60-64). One preferred technique utilizes an initiator that generates a free radical polymerization and vinyl monomers (see column 10 lines 10-17; instant claims 1, 9, 33, and 41-42). The resulting polymers are taught to be between 28 and 38 nm in length (see figure 3; instant claims 16 and 48). This technique is taught in particular in the production of patterned surfaces, where the initiator containing molecules are placed in particular locales on the substrate (see column 8 lines 53-64; instant claims 5 and 37). In one example, Hawker exemplifies the compound that makes up the linking layer as an initiator terminated alkanethiol that forms a patterned or continuous self assembled monolayer (column 13 lines 46-50 and 58-63; instant claims 4-7 and 36-39).

Since Chapman et al. and Zhang et al. teach particular chemical moieties on medical device surfaces to resist adsorption of undesired biological species upon implantation, it would have been obvious to one of ordinary skill in the art to combine their teachings. In addition, it also would have been obvious to combine the teachings of

Chapman et al. and Hawker et al. because both teach surface bound polymeric coatings attached via self assembled monolayers of reactive alkanethiol groups on metallic surfaces. Based upon these teachings it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare an orthopedic implant with the polymer layer of Chapman et al. via the method of Hawker et al. using an acrylate monomer coupled with tri(sarcosine) instead of the phosphorylcholine as taught by Zhang et al. (see instant claims 44-46). A free radical polymerization initiated from a self assembled monolayer of initiator-terminated alkanethiols on a gold surface would follow from this combination of references (see instant claim 48). Further modification of the resulting layer of polymer brush molecules by covalently attaching a protein (ligand), based upon the teachings of Chapman et al., would also have been obvious (see instant claims 18 and 50). Therefore claims 1-2, 4-9, 11-14, 16, 18-19, 21, 32-39, 41-46, 48, and 50 are obvious over Chapman et al. in view of Zhang et al. and Hawker et al.

Claims 1 and 28-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chapman et al. in view of Zhang et al. and Hawker et al. as applied to claims 1-2, 4-9, 11-14, 16, 18-19, 21, 32-39, 41-46, 48, and 50 above, and further in view of Healy (previously cited).

Chapman et al. in view of Zhang et al. and Hawker et al. make obvious an orthopedic device with a gold linking layer to which is attached a polymer brush composed of vinyl core monomers with tri(sarcosine) as head groups on its bristles (see instant claims 1-4, 6-9, 12-14, 18, 21, and 32). This modified reference does not



explicitly teach that the article is exposed to a particular biological fluid for a specified period of time.

Healy teaches that it was known at the time of the invention to covalently link RGD peptide sequences to the surface of protein resistant coatings to facilitate certain cell interactions (see page 383 column 2 paragraph 1). In particular these methods were envisioned for metal and polymer medical implants to facilitate wound healing (see page 348 column 1 paragraph 1). Wound healing would be an issue post-implantation where the implant contacts blood (e.g. orthopedic implant) and when it is present for a prolonged period (e.g. greater than one day). Thus it would have been obvious for one of ordinary skill in the art at the time of the invention to implant (*in vivo* contacting) the orthopedic device made obvious by Chapman et al. for longer than one day wherein during this period it was in contact with biological fluid and resisted protein adsorption. Therefore claims 1 and 28-31 are obvious over Chapman et al. in view of Zhang et al., Hawker et al., and Healy.

Claims 1, 17, 33, and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chapman et al. in view of Zhang et al. and Hawker et al. as applied to claims 1-2, 4-9, 11-14, 16, 18-19, 21, 32-39, 41-46, 48, and 50 above, and further in view of Leckband et al. (previously cited).

Chapman et al. in view of Zhang et al. and Hawker et al. make obvious an orthopedic device with a gold linking layer to which is attached a polymer brush composed of vinyl core monomers with tri(sarcosine) as head groups on its bristles (see

instant claims 1-4, 6-9, 12-14, 18, 21, and 32). This modified reference does not explicitly teach the surface density of polymer.

Leckband et al. teach polymer brushes on a substrate as a protein resistant surface (see abstract). In particular, Leckband et al. discuss that the graft density (polymer surface density) is a key parameter in controlling the degree of protein adsorption retardation (see page 1143 paragraph 4). Although Leckband et al. do not provide precise mass per area values for this parameter, they do teach that it is optimized based upon the target environment (e.g. size, geometry and concentration of proteins) (see page 1143 paragraph 4). Thus it would have been well within the purview of one of ordinary skill in the art to optimize such a parameter as a matter of routine experimentation. Therefore claims 1, 17, 33, and 39 are obvious over Chapman et al. in view of Zhang et al., Hawker et al., and Leckband et al.

Claims 33 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chapman et al. in view of Zhang et al. and Hawker et al. as applied to claims 1-2, 4-9, 11-14, 16, 18-19, 21, 32-39, 41-46, 48, and 50 above, and further in view of Guan et al. (previously cited)

Chapman et al. in view of Zhang et al. and Hawker et al. make obvious a method of making an orthopedic device with a gold linking layer to which is attached a polymer brush with tri(sarcosine) as head groups on its bristles, wherein the polymer brush is formed via surface initiated polymerization of monomers with a core monomer group and a protein resistant head group coupled thereto (see instant 33). This modified

reference does not explicitly teach that the polymerization is carried out via atom transfer radical polymerization.

Guan et al. teach that although it is known to polymerize vinyl monomers via free radical polymerization, atom transfer radical polymerization is also a means of polymerizing these same monomers (see column 1 lines 58-59 and column 2 lines 10-19). Thus as a known option within their technical grasp, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ atom transfer radical polymerization as the polymerization method instead of free radical polymerization in the invention of Chapman et al. in view of Zhang et al. and Hawker et al., where vinyl monomers are used as the core group. Therefore claims 33 and 40 are obvious over Chapman et al. in view of Zhang et al., Hawker et al., and Guan et al.

### ***Response to Arguments***

Applicants' arguments, filed August 18, 2009, have been fully considered but they are not deemed to be persuasive.

Applicants argue that there was no motivation to combine Chapman et al. with Zhang et al. and Hawker et al. Chapman et al. and Zhang et al. teach particular chemical moieties on medical device surfaces to resist adsorption of undesired biological species upon implantation, it would have been obvious to one of ordinary skill in the art to combine their teachings because both address the same issue. In addition, it also would have been obvious to combine the teachings of Chapman et al. and

Hawker et al. because both teach surface bound polymeric coatings attached via self assembled monolayers of reactive alkanethiol groups on metallic surfaces.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The rejections and/or objections detailed above are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

### ***Conclusion***

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CARALYNNE HELM whose telephone number is (571)270-3506. The examiner can normally be reached on Monday through Friday 9-5 (EDT).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Caralynne Helm/  
Examiner, Art Unit 1615

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